*Seizure* 2000; **9**: 291–293
doi: 10.1053/seiz.2000.0403, available online at http://www.idealibrary.com on IDEAL

SHORT COMMUNICATION

# A comparison of four new antiepileptic medications

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In order to select a new medication for a patient with epilepsy, it would be helpful to have an idea of which drug might have the greatest overall chance for success. Since epilepsy is a chronic disorder, the long-term effectiveness and tolerability of the medications are very important. Here, we compared gabapentin, lamotrigine, topiramate and vigabatrin using Kaplan–Meier survival analysis to see how long patients chose to stay on each drug and if they stopped, why they stopped. The results seem to suggest the type of responses to be expected in a hospital seizure clinic.



*Key words:* epilepsy; antiepileptics; comparison; seizures; side effects.

## INTRODUCTION

For complex partial seizures, several new drugs have become available in recent years. Each has its own mechanisms of action, benefits and side effects. With this in mind, a clinician must decide which to try first. One measure of a medication's success may be whether patients stay on it or not. This was a primary outcome used by Mattson *et al.*[1] in the two VA Cooperative studies comparing valproate to standard antiepileptic drugs (AEDs), in which duration of participation in the trial was considered a measure of the drugs' overall success in terms of efficacy and tolerable adverse effects.

While many studies have been done on each individual new AED as add-on therapy, few compare these relative newcomers with each other. Marson *et al.*[2] have performed meta-analyses comparing randomized placebo-controlled add-on trials of new AEDs in patients with partial epilepsy. They have provided an estimate of each drug's efficacy and tolerability compared with a placebo and then compared these estimates across drugs. Most recently, Wong *et al.*[3] analysed the long-term use of gabapentin (GBP), lamotrigine (LTG) and vigabatrin (VGB) in patients with chronic, primarily generalized and complex partial epilepsy. They used Kaplan–Meier survival analysis and Cox regression for comparison as well as using efficacy and incidence of side effects. Here, we look at the longevity of treatment in patients with complex partial epilepsy on GBP, LTG, topiramate (TOP) and VGB. These drugs were compared with each other using Kaplan–Meier survival analysis and, if they were discontinued, the reason was noted.

## METHODS

A retrospective chart review was conducted to include 61 refractory complex partial epilepsy patients from our current clinics who were on GBP, LTG, TOP or VGB. In most cases (83%) this included patients who had tried more than one new AED. These 61 subjects contributed 126 cases of new AED use. It was a pragmatic look at data from patients who were in open-label studies as well as on a marketed drug. We were looking to approximate the response one might be able to predict.

Sixty-four percent of the subjects were female with 36% male. They ranged in age from 20 to 84 years, with the majority between the ages of 30 and 50 years (mean age 43 years). Patients who had had surgery were not included. All patients were experiencing refractory complex partial seizures (ranging from 1 to 20 partial seizures per month) at the time a new AED was added. All medications were taken to the maximum tolerated dose if complete seizure control was not achieved. All were on at least one other seizure

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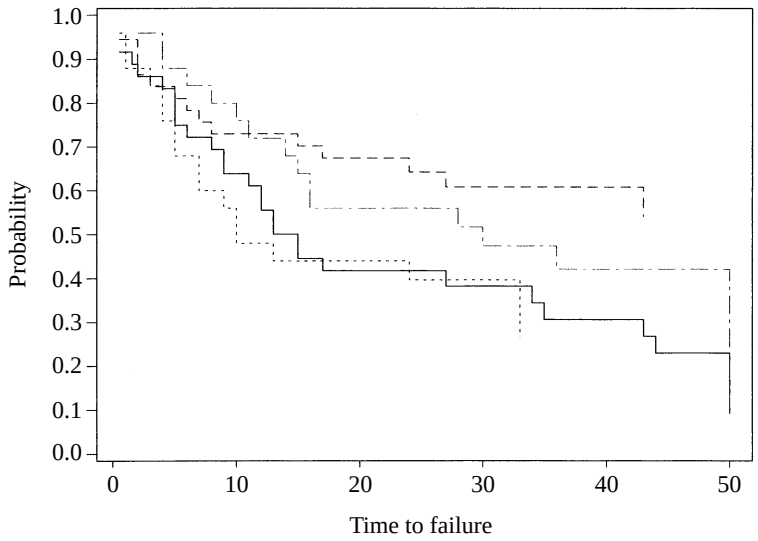


Fig. 1: Nonparametric survival plot for Gabapentin–Vigabatrin. Kaplan–Meier method, censoring column in C2–C8. ——, Gabopentin; – – –, lamotrigine; - - - -, topiramate; – · –, vigabatrin.

Table 1:

| | Results | | | |
|---|---|---|---|---|
| | Gabapentin | Lamotrigine | Topiramate | Vigabatrin |
| Number of patients | 36 | 37 | 28 | 26 |
| Time to 50% drop-out (median duration in months) | 13 | >43 | 9.5 | 29 |
| Percentages discontinued due to lack of efficacy | 21 (58%) | 9 (24%) | 7 (25%) | 16 (62%) |
| Percentages discontinued due to side effects | 8 (22%) | 6 (16%) | 7 (25%) | 3 (12%) |
| Continuing | 7 (19%) | 22 (60%) | 14 (50%) | 7 (27%) |

medication prior to starting their new AED. All subjects were under the care of the same physician in the same location. Almost all had onset of epilepsy in childhood.

We looked at the length of time patients used each medication and the primary reason for discontinuation, if they did not continue new AED therapy. A survival analysis was performed for each drug using the Kaplan–Meier method. Time to failure was the variable and patient data were censored if continuing on therapy at the time of data collection (Fig. 1).

The most common side effect of TOP was severe irritability, which occurred in seven out of ten discontinuations due to side effects. The side effects reported for all drugs included the usual CNS symptoms which are commonly associated with the established AEDs, for example: dizziness, tiredness, difficulty thinking, weight gain and occasional rash (two GBP and three LTG). Loss of efficacy over time was as common with VGB as lack of efficacy from the outset; this was included as half of the discontinuations due to lack of efficacy.

## RESULTS

See Table 1.

## DISCUSSION

Although these numbers are small, the data do suggest some information. Lamotrigine appeared to be least likely to be discontinued by a rather wide margin. Its low rate of side effect discontinuation and strong efficacy combine to make it the drug that more patients have taken the longest in our clinic. Topiramate seemed equally efficacious, with the most dropouts out of all the drugs due to side effects. And, while GBP and VGB appear equally matched with each other for efficacy, VGB had the fewest side effects determining drop-out of all the new drugs.

Recently, Wong *et al.*[3] have suggested that patients with both primary and complex partial epilepsy were

less likely to stop LTG therapy than GBP or VGB. In the past, Marson *et al.*[4] have concluded in their meta-analysis that LTG seemed least likely to be discontinued. McDonnell and Morrow[5] in their audit of GBP, LTG and VGB showed similar results for these drugs. They also saw evidence of tolerance with VGB.

Crawford[6] has found the incidence of psychiatric symptoms significantly higher in patients taking TOP, and an overall dropout due to side effects (41%) which was significantly higher than ours. But incidence of these adverse effects could be reduced by using 25 mg dose increments. Our patients had been titrated slowly for TOP and all of the other drugs except VGB, which we had been able to start immediately at a maintenance dose (3 g) without any problem in many patients.

In general, our findings support those of other researchers in hospital clinic settings.

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